Claims

1. A method of inducing or enhancing the expression of granzyme B in natural killer (NK) cells comprising contacting NK cells with
   (a) Hsp70 protein;
   (b) a (C-terminal) fragment of (a) comprising the amino acid sequence TKDNNLLGRFELSG;
   (c) a (poly)peptide comprising the amino acid sequence TKDNNLLGRFELSG; or
   (d) a combination of (a), (b) and/or (c).

2. The method of claim 1, wherein the Hsp70 protein, the (C-terminal) fragment thereof, the (poly)peptide comprising the amino acid sequence TKDNNLLGRFELSG, or the combination thereof is in an uncomplexed state.

3. The method of claim 1 or 2, which is an in vivo method.

4. The method of claim 1 or 2, which is an ex vivo method.

5. The method of claim 1 or 2, which is an in vitro method.

6. The method of claim 4 further comprising reinfusion of NK cells with induced or enhanced granzyme B expression into a mammal.

7. The method of claim 6, wherein the reinfused NK cells are autologous and/or allogeneic NK cells.

8. The method of claim 6 or 7, wherein said mammal is a human.

9. The method of any one of claims 1 to 8 wherein said contacting is effected for at least 12 hours.

10. The method of claim 9, wherein said contacting is effected for at least 4 weeks.

11. The method of any one of claim 1 to 10 wherein said NK cells are prior to said contacting, obtained from bone marrow by incubating said bone marrow cells with interleukin-15 (IL-15) and stem cell factor (SCF) at concentrations of 1ng/ml – 1000 ng/ml per cytokine for at least 7 days up to 4 months.

12. Use of NK cells which produce granzyme B after stimulation with

(a) Hsp70 protein;

(b) a (C-terminal) fragment of (a) comprising the amino acid sequence TKDNNLLGRFELSG;

(c) a (poly)peptide comprising the amino acid sequence TKDNNLLGRFELSG; or

(d) a combination of (a), (b) and/or (c);

for the preparation of a pharmaceutical composition for the treatment of tumors, viral or bacterial infections or inflammatory diseases.

13. The use according to claim 12 wherein the NK cells are stimulated by a method according to any of claims 1 to 11.

14. Use of granzyme B for the preparation of pharmaceutical composition for the perforin-independent treatment of tumors, viral or bacterial infections or inflammatory diseases.

15. The use of claim 14 wherein granzyme B is used as the only pharmaceutically active compound in said pharmaceutical composition.

16. A method of treating tumor, viral or bacterial infections or inflammatory

diseases comprising of:

(a) contacting NK-cells with tumor cells bearing Hsp70 on their surface or cells affected by said infection or inflammation and bearing Hsp70 on their surface;

(b) allowing granzyme B to enter said cells via ion channels formed by said Hsp70 on the cell surface; and

(c) allowing said cells to undergo apoptosis as a result of the enzymatic activity of granzyme B.

17. A method treating tumor, viral or bacterial infections or inflammatory diseases comprising of:

(a) contacting tumor cells bearing Hsp70 on their surface or cells affected by said infection or inflammation and bearing Hsp70 on their surface with granzyme B;

a. allowing granzyme B to enter said cells via ion channels formed by said Hsp70 on the cell surface; and

b. allowing said cells to undergo apoptosis as a result of the enzymatic activity of granzyme B.

18. The method of claim 16 or 17, wherein granzyme B is administered in a final concentration of 1μg/ml to 500μg/ml.

19. The method of claim 16 or 17, wherein granzyme B is administered in a final concentration of 1ng/ml to 10 ng/ml.

20. The method of claim 19 wherein granzyme B is administered in a final concentration of about 6 ng/ml.

21. The use of claim 14 or 15 or the method of any one of claims 16 to 20

wherein granzyme B is packaged in liposomes.

22. The use of any one of claims 12 to 15 or 21 wherein said tumors comprise tumor cells which express Hsp70 on the surface of their membrane or wherein cells affected by said infection or inflammation express Hsp70 on the surface of their membrane.

23. The use of any one of claims 12 to 15, 21 or 22 or the method of any one of claims 16 to 22, wherein said tumors are selected from a group consisting of stomach, gastric, colorectal, lung, pancreas, mammary, gynecological, head and neck tumors, dermatological tumors (e.g. melanoma), neuronal tumors, leukemia and lymphoma.

24. The use of any one of claims 12 to 15, 21 or 22 or the method of any one of claims 16 to 22, wherein the viral infection is an infection by HIV or Hepatitis virus.